

## Remarks

Claims 1, 10, 27, 31, and 32 have been amended. Claims 1 to 10 and 26 to 32 are pending and under consideration. Claims 11 to 25 are also pending, but have been withdrawn from consideration.

Support for the amendments to claims 1, 10, 27, 31, and 32 is found in the specification, e.g., at pages 13 and 14, paragraph 44. Thus, the claims are fully supported by the specification and add no new matter.

## Rejection in View of Drmanac and Gingeras

The Examiner rejected claims 1 to 10 and 26 to 32 under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,309,824 ("Drmanac"), in view of U.S. Patent No. 6,228,575 ("Gingeras"). See Final Action, at page 3. Applicants respectfully traverse.

At the outset, applicants would like to clarify their understanding of the Final Action. In the Final Action, the 35 U.S.C. § 103(a) rejection of the claims as allegedly being unpatentable over Drmanac in view of Gingeras ("the § 103 rejection"), is a rejection repeated from the Office Action mailed April 8, 2004 ("April 2004 Action"), at pages 3 to 5, item 4. However, the § 103 rejection in the Final Action deletes most of the text of the corresponding rejection from the April 2004 Action. That text concerned the Examiner's allegations concerning certain elements of the claims. The current § 103 rejection only includes a response to one of applicants' arguments, and includes almost no discussion of the elements of the rejected claims. Applicants, however, will

respond to the Final Action as if all of the text of the § 103 rejection at item 4 of the April 2004 Action was reiterated in the Final Action.

For a proper obviousness rejection, the Examiner must establish that the cited documents would have suggested all of the claim elements to one of ordinary skill. See MPEP § 2143.03.

As applicants pointed out in the Response filed on July 8, 2004 ("the July 2004 Response"), the Examiner failed to address all of the elements of all of the claims in the April 2004 Action. Instead of responding to all of applicants' arguments, the Examiner only responds to applicants' arguments concerning independent claims 1, 10, 27, 31, and 32. The Examiner fails to address applicants' other separate arguments concerning independent claims 26 and 30. Nor does the Examiner explain how the cited documents would have suggested all of the claim elements of all of those claims to one of ordinary skill in the art.

If the Examiner chooses to maintain this rejection, applicants respectfully request that the Examiner address ***all of the elements*** of ***all of the claims***, and that the Examiner respond to all of applicants' arguments concerning those claims.

#### **Independent Claim 1**

In the Examiner's rejection of claims 1 to 10 and 26 to 32 in the April 2004 Action, the Examiner did not specifically address the claim language of the rejected claims. See April 2004 Action, at page 3. Nor did the Examiner specifically point out how Drmanac and Gingeras would have suggested all of the elements of the rejected claims. Instead, the Examiner appeared to cite language from the abstract of Drmanac and certain other unspecified sections of Drmanac, and then implied that the cited

sections show certain aspects of the claims by acknowledging that Drmanac did not show certain other elements of certain claims. See April 2004 Action at pages 3 to 4.

In the July 2004 Response, applicants asserted that the cited sections of Drmanac do not describe a method according to claim 1, which comprises “exposing a substrate containing a first feature comprising an experimental target-specific probe and a control-specific probe to a labeled control target, such that the labeled control target binds specifically to control-specific probe bound to the substrate....” Specifically, the cited sections of Drmanac discuss a method comprising two probes and a target nucleic acid sequence. See April 2004 Action at page 3. One probe is attached to a substrate (“the attached probe”). See *id*. The second probe comprises a label (“the labeled probe”). See *id*. The target nucleic acid sequence comprises two adjacent portions. See *id*. The probes and nucleic acids are treated such that the first portion of the target nucleic acid hybridizes to the attached probe and the second portion of the target nucleic acid hybridizes to the labeled probe. See *id*. After hybridization of both probes, the probes are affixed, and the labeled probe, which is now fixed to the array, is detected. See *id*.

Furthermore, applicants asserted that even if the labeled probe of Drmanac is incorrectly construed as a labeled control target, Drmanac still fails to show “exposing a substrate containing a first feature comprising an experimental target-specific probe and a control-specific probe to a labeled control target, such that the labeled control target binds specifically to control-specific probe bound to the substrate....” Specifically, applicants asserted that the labeled probe of Drmanac specifically hybridizes to the target nucleic acid sequence, which is not bound to the substrate. See *id*. Thus, even if

the labeled probe of Drmanac is incorrectly characterized as a labeled control target and the target nucleic acid is incorrectly characterized as a control specific probe, Drmanac still does not show a labeled control target binding to a control specific probe bound to the substrate.

In response to applicants' arguments, the Examiner argued that the probes affixed to the substrate of Drmanac are target specific probes. See Final Action at page 3. The Examiner also argued that the target nucleic acid of Drmanac is a control specific probe, and the labeled probe of Drmanac is a labeled control target. See *id*. The Examiner then concluded that "...the target of Drmanac is viewed to be indirectly bound to the substrate before adding the labeled probe." See *id*.

Solely to expedite prosecution, and without acquiescing to the Examiner's rejection, applicants have amended claim 1 to include the language "wherein the control-specific probe is not bound to the substrate by hybridization." In Drmanac, the target nucleic acid is hybridized to the probes that are affixed to the substrate. Thus, even if one incorrectly considers the target nucleic acid to be a control-specific probe, as suggested by the Examiner, it is hybridized to another nucleic acid that in turn is affixed to the substrate. Thus, Drmanac would not have suggested a "control-specific probe bound to the substrate, wherein the control-specific probe is not bound to the substrate by hybridization." Therefore, the amendment to claim 1 obviates the Examiner's rejection.

Gingeras would have failed to remedy at least that deficiency of Drmanac. Accordingly, for at least that reason, the Examiner has failed to establish that claim 1 would have been obvious over Drmanac in view of Gingeras. Claims 2 to 9 depend

from claim 1. Thus, for the reasons discussed above for claim 1, the Examiner fails to establish that claims 2 to 9 would have been obvious over Drmanac in view of Gingeras.

Because Gingeras would have failed to remedy the deficiency of Drmanac, applicants need not address the Examiner's allegations regarding Gingeras. Also, because the Examiner fails to establish that claims 1 to 9 would have been obvious for at least the reasons discussed above, applicants need not address the Examiner's contentions concerning other elements of those claims. By not addressing those contentions, applicants in no way acquiesce to those contentions.

Applicants respectfully request reconsideration and withdrawal of the § 103 rejection of claims 1 to 9 over Drmanac in view of Gingeras.

**Independent Claim 10**

In the rejection of claims 1 to 10 and 26 to 32 in the April 2004 Action, the Examiner did not specifically address the claim language of the rejected claims. See April 2004 Action, at page 3. Nor did the Examiner specifically point out where Drmanac would have suggested the elements of the rejected claims. Instead, the Examiner appeared to cite language from the abstract of Drmanac and certain other unspecified sections of Drmanac, and then implied that the cited sections show certain aspects of the claims by acknowledging that Drmanac does not show certain other elements of certain claims. See April 2004 Action at pages 3 to 4.

As discussed above, the cited sections of Drmanac discuss a particular orientation of two probes and a target such that a first probe attached to a substrate binds a target nucleic acid sequence, which is bound by a second labeled probe. In the July 2004 Response, applicants asserted that the cited sections of Drmanac would not

have suggested a method according to claim 10, which comprises “exposing a substrate containing a feature comprising an experimental target probe to a labeled control target and a labeled experimental target, such that the labeled control target binds to experimental target probe bound to the substrate....”

Furthermore, applicants asserted that even if the labeled probe of Drmanac is incorrectly construed as a labeled control target, Drmanac still fails to show “exposing a substrate containing a feature comprising an experimental target probe to a labeled control target and a labeled experimental target, such that the labeled control target binds to experimental target probe bound to the substrate....” Specifically, applicants asserted that Drmanac would not have suggested a method wherein “the labeled control target binds to experimental target probe bound to the substrate....”

In the Final Action, the Examiner responded to those arguments by arguing that the target of Drmanac is indirectly bound to the substrate.

Solely to expedite prosecution, and without acquiescing to the Examiner’s rejection, applicants have amended claim 10 to include the language “wherein the experimental target probe is not bound to the substrate by hybridization.” In Drmanac, the target nucleic acid is hybridized to the probes that are affixed to the substrate. Thus, even if one incorrectly considers the target nucleic acid to be a control-specific probe, as suggested by the Examiner, it is hybridized to another nucleic acid that in turn is affixed to the substrate. Thus, Drmanac does not discuss an “experimental target probe bound to the substrate, wherein the experimental target probe is not bound to the substrate by hybridization.” Therefore, the amendment to claim 10 should obviate the Examiner’s rejection

Gingeras would have failed to remedy the deficiencies of Drmanac. Accordingly, for at least that reason, the Examiner has failed to establish that claim 10 would have been obvious over Drmanac in view of Gingeras.

Because Gingeras would have failed to remedy the deficiency of Drmanac, applicants need not address the Examiner's allegations regarding Gingeras. Also, because the Examiner fails to establish that claim 10 would have been obvious for at least the reasons discussed above, applicants need not address the Examiner's contentions concerning other elements of claim 10. By not addressing those contentions, applicants in no way acquiesce to those contentions.

Applicants respectfully request reconsideration and withdrawal of the § 103 rejection of claim 10 over Drmanac in view of Gingeras.

**Independent Claims 27, 31, and 32**

As discussed above, the Examiner did not specifically address the claim language of the rejected claims. See April 2004 Action, at page 3. Nor did the Examiner specifically point out where Drmanac would have suggested the elements of the rejected claims. Instead, the Examiner appeared to cite language from the abstract of Drmanac and certain other unspecified sections of Drmanac, and then implied that the cited sections show certain aspects of the claims by acknowledging that Drmanac does not show certain other elements of certain claims. See April 2004 Action at pages 3 to 4.

As discussed above, the cited sections of Drmanac discuss a particular orientation of two probes and a target such that a first probe attached to a substrate binds a target nucleic acid sequence, which is bound by a second labeled probe. In the

July 2004 Response, applicants asserted that the cited sections of Drmanac would not have suggested methods according to claims 27, 31, and 32, which comprise “exposing a substrate containing a first feature comprising an experimental target-specific probe and a control-specific probe to a labeled control target and a labeled experimental target, such that the labeled control target binds specifically to control-specific probe bound to the substrate....”

Furthermore, applicants asserted that even if the labeled probe of Drmanac is incorrectly construed as a labeled control target, Drmanac still would have failed to suggest “exposing a substrate containing a first feature comprising an experimental target-specific probe and a control-specific probe to a labeled control target and a labeled experimental target, such that the labeled control target binds specifically to control-specific probe bound to the substrate....” Specifically, applicants asserted that Drmanac does not show a method wherein “the labeled control target binds specifically to control-specific probe bound to the substrate....”

In the Final Action, the Examiner responded to those arguments by arguing that the target of Drmanac is indirectly bound to the substrate.

Solely to expedite prosecution, and without acquiescing to the Examiner’s rejection, applicants have amended claims 27, 31, and 32 to include the language “wherein the control-specific probe is not bound to the substrate by hybridization.” In Drmanac, the target nucleic acid is hybridized to the probes that are affixed to the substrate. Thus, even if one incorrectly considers the target nucleic acid to be a control-specific probe, as suggested by the Examiner, it is hybridized to another nucleic acid that in turn is affixed to the substrate. Thus, Drmanac does not discuss a “control-

specific probe bound to the substrate, wherein the control-specific probe is not bound to the substrate by hybridization.” Therefore, the amendments to claims 27, 31, and 32 should obviate the Examiner’s rejections.

Gingeras would have failed to remedy at least that deficiency of Drmanac. Accordingly, for at least this reason, the Examiner has failed to establish that claims 27, 31, and 32 would have been obvious over Drmanac in view of Gingeras. Claims 28 and 29 depend from claim 27. Thus for the reasons discussed above for claim 27, the Examiner fails to establish that claims 28 and 29 would have been obvious over Drmanac in view of Gingeras.

Because Gingeras fails to remedy that deficiency of Drmanac, applicants need not address the Examiner’s allegations regarding Gingeras. Also, because the Examiner fails to establish that claims 27 to 29, 31, and 32 would have been obvious for at least the reasons discussed above, applicants need not address the Examiner’s contentions concerning other elements of those claims. By not addressing those contentions, applicants in no way acquiesce to those contentions.

Applicants respectfully request reconsideration and withdrawal of the § 103 rejection of claims 27 to 29, 31, and 32 over Drmanac in view of Gingeras.

#### **Independent Claims 26 and 30**

As discussed above, the Examiner did not specifically address the claim language of the rejected claims. See April 2004 Action, at page 3. Nor did the Examiner specifically point out where Drmanac would have suggested the elements of the rejected claims. Instead, the Examiner appeared to cite language from the abstract of Drmanac and certain other unspecified sections of Drmanac, and then implied that

the cited sections show certain aspects of the claims by acknowledging that Drmanac does not show certain other elements of certain claims. See April 2004 Action at pages 3 to 4.

Claims 26 and 30 include the language “determining the ratio of the intensity of the signal from the first label to the intensity of the signal from the second label for each of the first and second features; and comparing the ratios of the intensity of the signal for the first and second features to calculate the relative amount of first and second experimental... target sequences in the sample.” In the July 2004 Response, applicants asserted that the Examiner did not specifically address those elements of claims 26 and 30. Furthermore, applicants asserted that Drmanac would have failed to show those elements of claims 26 and 30.

Specifically, applicants argued that the cited sections of Drmanac discuss “detecting the labeled probe affixed to the probe in the array” and “determining the presence of the sequenced gene by detection of labeled probes bound to prespecified locations in the array.” See April 2004 Action at pages 3 to 4. That language would have failed to suggest “determining the ratio of the intensity of the signal from the first label to the intensity of the signal from the second label for each of the first and second features; and comparing the ratios of the intensity of the signal for the first and second features to calculate the relative amount of first and second experimental... target sequences in the sample.” That language is included in claims 26 and 30.

In the Final Action, the Examiner did not respond to those arguments. Instead, the Examiner only responded to applicants’ arguments concerning claim 1. That particular argument concerned the orientation of probes and targets in claim 1.

Applicants argument concerning claims 26 and 30 discussed elements of those claims concerning calculating the relative amount of first and second experimental target sequences in the sample. The Examiner has not responded to those arguments. Nor has the Examiner otherwise described how the cited documents would have suggested those elements of claims 26 and 30. If the Examiner chooses to maintain this rejection, applicants request that the Examiner address applicants' arguments concerning claims 26 and 30.

For those reasons, the Examiner failed to establish that Drmanac would have suggested "determining the ratio of the intensity of the signal from the first label to the intensity of the signal from the second label for each of the first and second features; and comparing the ratios of the intensity of the signal for the first and second features to calculate the relative amount of first and second experimental... target sequences in the sample."

Gingeras would have failed to remedy the deficiencies of Drmanac. Accordingly, for at least this reason, the Examiner has failed to establish that claims 26 and 30 would have been obvious over Drmanac in view of Gingeras.

Because Gingeras fails to remedy the deficiency of Drmanac, applicants need not address the Examiner's allegations regarding Gingeras. Also, because the Examiner fails to establish that claims 26 and 30 would have been obvious for at least the reasons discussed above, applicants need not address the Examiner's contentions concerning other elements of those claims. By not addressing those contentions, applicants in no way acquiesce to those contentions.

Applicants respectfully request reconsideration and withdrawal of the § 103 rejection of claims 26 and 30 over Drmanac in view of Gingeras.

**Conclusion**

Applicants respectfully assert that the application is in condition for allowance and request issuance of a Notice of Allowance. If the Examiner does not consider the application to be in condition for allowance, applicants request that the Examiner call the undersigned at (650) 849-6658 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: December 13, 2004

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